IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IBERT C. WELLS	)	
	)	Examining Attorney:
Serial No. 10/805,881	)	Michael Edward Szperka
	)	
Filed: 3/22/04	)	Art Group: 1644
	)	
METHODS FOR DETECTING DEFICIENT CELLULAR MEMBRANE TIGHTLY BOUND MAGNESIUM FOR DISEASE DIAGNOSES	)	

DECLARATION UNDER RULE 1.132

DECLARATION A

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Ibert C. Wells, do hereby declare and state as follows:

1. I am the same Ibert C. Wells named as Inventor on the above referenced patent application.

2. I graduated from Central Methodist College, Fayette, Missouri in 1942 with an AB in chemistry.

3. I received my PhD from St. Louis University in 1948 in the field of biochemistry, studying under Nobelist E. A. Doisy.

4. From 1948 to 1950 I held a Post-Doctoral Fellowship from the National Science Foundation under Linus Pauling, a two time Nobelist at the California Institute of Technology in Pasadena, California. Pauling is a leader in the study of the structure of molecules. See: Linus Pauling; *The Nature of the Chemical Bond and the Structure of Molecules and Crystals,* third ed., Cornell University Press, 1960, Ithaca New York.

5. From 1950 to 1960 I was employed as an instructor and associate professor at the State University New York, Upstate Medical Center, in Syracuse, New York in the Department of Biochemistry.

6. From 1960 to 1975 I was employed by Creighton University, Omaha, Nebraska in several capacities, including Chairman of the Department of Biochemistry and Professor of Biochemistry.

7. I have worked in the field of biochemistry for more than sixty years.

8. Based on my experience, I am knowledgeable of the average skill of biochemists.

9. I am familiar with the Office Action mailed on December 16, 2005, in connection with the above-referenced patent application. In that Office Action the Examiner asserts that the specification is deficient in teaching how to use the invention, in part, because Applicant has not demonstrated that lower levels of the amidated peptides of SEQ ID NOs: 1, 2, and 4 in plasma of a rat model of magnesium binding defect as compared to levels of such peptides in controls.

10. While not wishing to be limited to a particular mode of action or explanation of how the invention works, the following is offered as background of the technology and description of a possible correlation between preeclampsia, essential hypertension, and type 2 diabetes.

11. Preeclampsia is a consequence of normal pregnancy imposition on type 2 diabetes syndrome.

12. Implications that follow:

a. Type 2 diabetes syndrome has the capability of altering the physiology of normal pregnancy.

b. Pregnancy altering capability of type 2 diabetes must exist in/or during the physiological mechanism causing type 2 diabetes which can alter the physiology and biochemistry and/or physiology of pregnancy. These mechanisms and their results are inherent to type 2 diabetes.

c. Changes from normal physiology evident in type 2 diabetes include: 1) essential hypertension; 2) diabetes mellitus, 3) the magnesium binding defect (MgBD) or decreased intracellular [Mg^{2+}] and its dependent [$MgATP^{2}$]. Of these number 3) is primary.

d. MgBD, signifies a decrease (perhaps variable) in the concentration of Mg^{2+} in the cell membranes of somatic cells and causes increased passive permeability of the cell membrane to sodium ions and decreased entrance of Mg^{2+} and $MgATP^{2-}$ ions into the cell.

e. As disclosed in the above-referenced patent application; the MgBD is caused by decreased concentration of Mg^{2+} binding promoters in the plasma. The MgBD is believed to be inherited.

f. In order for Mg^{2+} and $MgATP^{2-}$ ions to enter the cell, Mg^{2+} ions must bind to the cell membrane. The MgBD signifies that this situation has not occurred to the normal degree.

g. The binding of the Mg^{2+} ions to the cell membrane requires the "magnesium binding promoters" which occur in normal plasma and have been discovered to include the amidated pentapeptide and its contained amidated tetrapeptide. These peptides have the same amino acid sequence as the carboxy terminus of Substance P. Substance P is

synthesized in the forebrain from which it is believed the binding promoters are released by the enzyme enkephalinase, which also occurs in the forebrain. It is apparent that the binding promoters can cause variable amounts of Mg^{2+} ions to bind to the cell membrane depending on the concentrations of binding promoters, Mg^{2+} ions and somatic cells.

h. Thus the Mg^{2+} ion bound to the somatic cell membrane is a variable quantity which is not believed to be solely dependent on the concentration of "magnesium binding promoters."

i. Thus, the measurement of bound Mg^{2+} ions is not reliable as the only measure of the concentration of Mg^{2+} binding promoters.

j. Therefore, specific assays for the Mg^{2+} binding promoters must be used.

12 I further state that all statements made herein are true and that these statements are made with the knowledge that willful false statements and the like are punishable by fine or imprisonment or both under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the patent application and any issued patent resulting therefrom.

June 16, 2004
Dated

Ibert C. Wells